

Case Report

Extrahepatic undifferentiated embryonal sarcoma, cytology as an accurate method for early diagnosis: an extremely rare case report in an Indian child

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Received: 08 June 2019

Revised: 14 June 2019

Accepted: 03 July 2019

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ABSTRACT

Undifferentiated embryonal sarcoma has been described in the liver, a rare malignant mesenchymal neoplasm, that occurs primarily in children and teenagers. Approximately 260 cases have been reported arising in the liver since 1978 when this disease was first described. Its pathogenesis is still obscure. Authors presented a case of extrahepatic undifferentiated embryonal sarcoma in a 9-year-old female presenting with upper abdominal dull pain. Ultrasound and CT Scan showed normal liver architecture, with liver pushed upwards due to compression by tumor arising in the retroperitoneum. To the best of our knowledge, this is first case of extrahepatic undifferentiated embryonal sarcoma diagnosed on cytomorphology and confirmed by histopathology and immunohistochemistry markers.

Keywords: Child, Extrahepatic, First case, Undifferentiated embryonal sarcoma

INTRODUCTION

The present case diagnosed as Extrahepatic undifferentiated embryonal sarcoma is the first case, hence there are no references and literature available. Undifferentiated embryonal sarcoma of liver (UESL) although a rare entity in itself, its literature and references available pertain to the UESL. Undifferentiated embryonal sarcoma of liver (UESL) is a unique tumor type, first described by Willis as rhabdomyoblastic mixed tumor in childhood.^{1,2} Willis differentiated UES from two reports on embryonal rhabdomyosarcoma of the extrahepatic bile ducts. In 1973, Stanley and associates reported 3 cases of UES, with diagnosis of malignant mesenchymoma, this study was then followed by a study of 31 cases by Stocker and Ishak, who proposed the designation undifferentiated embryonal sarcoma. It

affects most frequently children between the ages of 6-10 years, uncommon in adults.^{3,4} Rarely it has been reported in adults showing female predominance, oldest reported by Ellis and Cotton in 1983, in patient aged 86 year old female.⁵⁻⁷ UESL represents 5-13% of all pediatric uncommon hepatic tumors, approximately 260 cases have been reported in the literature.⁸ UES is the 3rd most common malignant tumor of the liver in children after hepatoblastoma, 88% of cases occurring in <15 years age. UES most often affects the right lobe of liver; distant metastases are rare. It presents with right upper quadrant abdominal mass, anorexia and intermittent fever.

Two theories have been suggested. There is a link between UES and mesenchymal hamartoma of the liver (MHL) and link between progenitor ship or histogenesis of this neoplasm. Relationship between UES and MHL is

based on two reports in the literature which shares genetic aberration in the UES and MHL.²

Pre-operative clinical diagnosis of undifferentiated embryonal sarcoma is difficult due to lack of characteristic clinical presentation, serological markers and radiological changes.

CASE REPORT

A 9 year old Indian female presented with dull upper abdominal pain for almost 1 month. At presentation ultrasonography showed a well-defined subhepatic heterogenous mass measuring 10.6 x 7 cm with central necrotic areas. Ultrasound guided Fine Needle aspiration was done. The smears were air dried and stained with Giemsa. Cytosmears revealed a combination of polygonal and spindle cells. Polygonal cells were large, with round nuclei and occasional multinucleated, with one or several nucleoli and variable cytoplasm with poorly defined borders. A few intracytoplasmic and extra cytoplasmic eosinophilic globules were seen.

Myxoid areas were seen at places. According to the cytomorphology diagnosis of Undifferentiated embryonal sarcoma was made (Figure 1). Laboratory investigations like liver function tests, renal function tests, alpha feto protein, Beta -HCG, LDH were within normal range.

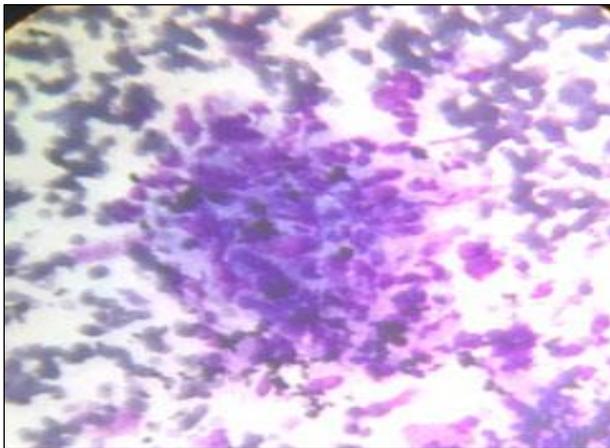


Figure 1: Cytosmear, MGG stain, 40 X, polygonal to spindle shaped cells.

To confirm the cytological findings, Ultrasound guided tru cut needle biopsy was done. H and E stained slides of histopathological sections revealed loose myxoid stroma with stellate to spindle shaped cells showing hyperchromatic nucleus. Many cells showed bubbly vacuolated cytoplasm and few giant cells. Large ectatic vascular spaces were interspersed. Few cells showed PAS positive pink globules. No bile ductular structures or hepatocytic cells were seen. Histological diagnosis was consistent with the cytomorphological diagnosis of Undifferentiated embryonal sarcoma (Figure 2). To confirm the diagnosis Immunohistochemistry was done

which showed diffuse positivity of Vimentin (Figure 3), Desmin was focally positive in giant cells. CD 10 (Figure 4), CD68 (Figure 5), Calponin (Figure 6) showed positivity. SMA, LCA was focally positive.

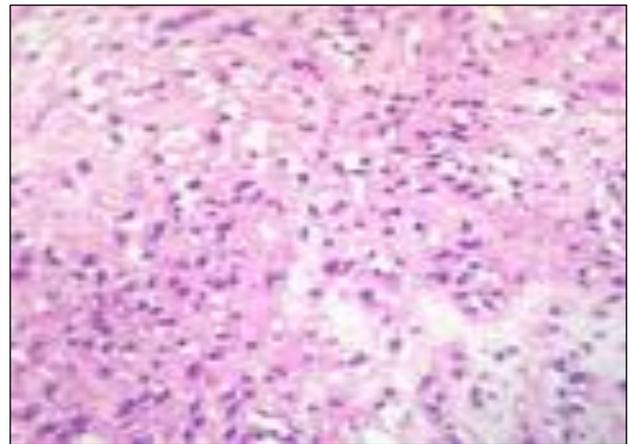


Figure 2: H and E, biopsy, 40 x, stellate to spindle cells, myxoid background.

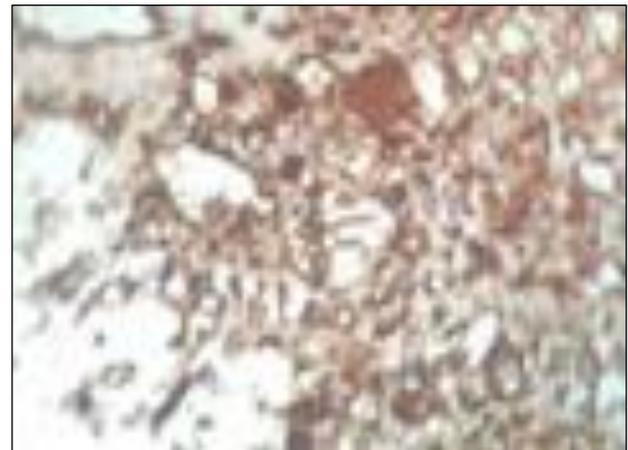


Figure 3: Vimentin, diffuse positive.

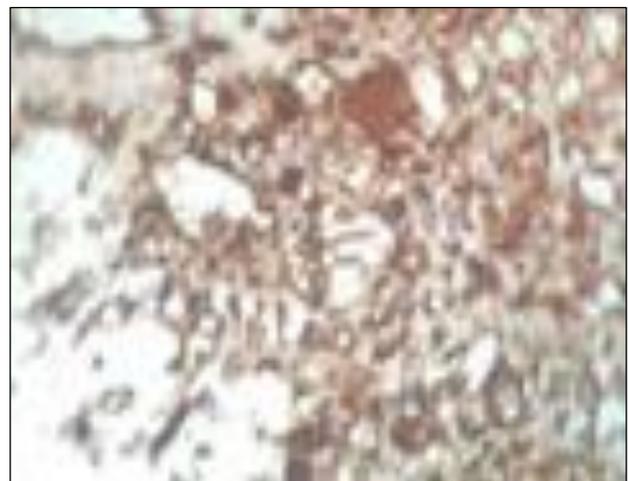


Figure 4: CD 10, positive.

Bcl-2 (Figure 7) showed positivity in majority of cells. CD 34 showed positivity in large ectatic and small vascular walls. CK, S 100, Myo D1, AFP, CK 19, CK 7 were all negative. B-Catenin showed negative nuclear stain but membranous positivity. Based on IHC markers, Diagnosis of Undifferentiated embryonal sarcoma was established.

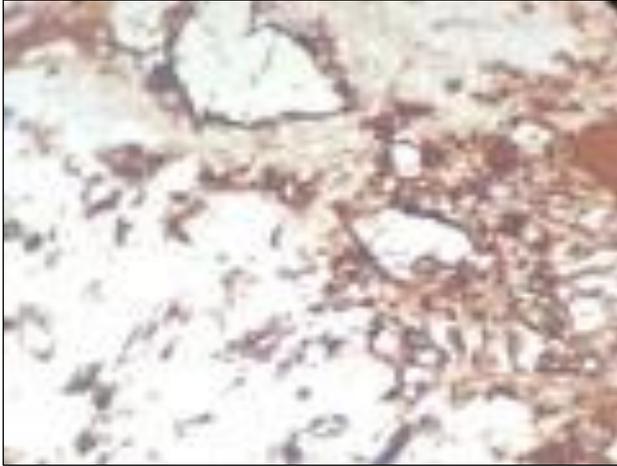


Figure 5: CD 68, positive.



Figure 6: Calponin, positive.

Patient turned up for the reports 1 month later. CT scan of abdomen was done to know the extent of tumor, which showed significant enlarged vascular soft tissue mass measuring 200 x 130 mm with internal necrotic area occupying whole right side of abdomen from subhepatic to iliac region. The mass was seen compressing and displacing the liver superiorly with minimal IHBR compression and dilatation. No internal fat or calcification was seen (Figure 8).

Kidneys were free from tumor. Gall bladder, spleen, pancreas was normal. Following the treatment guidelines for UESL, multimodal therapy was planned but as the tumor was large and patient general condition was poor, surgical excision of the tumor could not be done.

Chemotherapy was started with injection Cyclophosphamide 750 mg/m², injection Doxorubicin 50 mg/m², injection Vincristine 1.4 mg/m² every 3 weekly with GCSF support to which the patient responded.

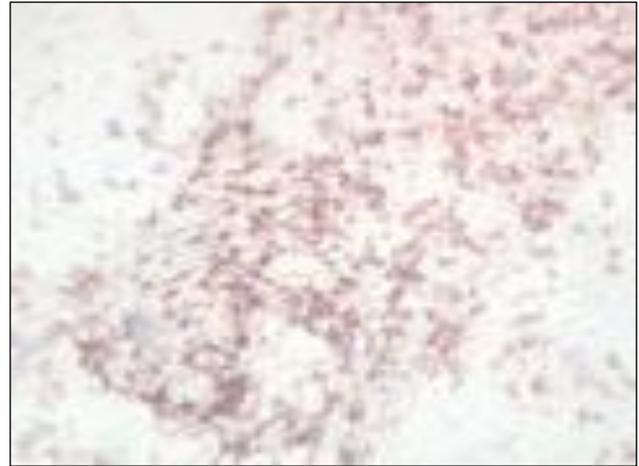


Figure 7: Bcl 2, positive in majority of cells.



Figure 8: CT Scan, soft tissue mass measuring 200x130 mm with internal necrotic area occupying whole right side of abdomen from subhepatic to iliac region.

DISCUSSION

As the present case is the first to be diagnosed as extrahepatic undifferentiated embryonal sarcoma, the references and literature available are those of undifferentiated embryonal sarcoma of liver (UESL).

UESL is a rare and aggressive mesenchymal neoplasm occurring in children and adolescents. It was previously reported as mesenchymoma, mesenchymal sarcoma, embryonal sarcoma, fibrosarcoma, primary sarcoma of the liver. In 1978, Stocker and Ishak distinguished UESL from other sarcoma.³ UESL occurs in children 6-10 years of age, rare after 15 years of age. It accounts for 5-8% of

hepatic tumors in children. About 260 cases have been reported, with 14 cases above 60 years of age.^{8,9} Clinical symptoms are non-specific, including abdominal mass with or without abdominal pain, fever, nausea, vomiting, weight loss, fatigue, jaundice. Occasionally, spontaneous rupture may cause intraperitoneal haemorrhage.^{10,11} There are no specific laboratory investigations for this tumor. AFP, CA19-9, CEA are usually within normal limits, occasionally AFP may be elevated.¹²

Radiological findings are also not specific. The complex cystic lesion because of high water content may lead to mistaken diagnosis of hydatid cyst or benign lesion.¹³ On ultrasound, a large mass that may be predominantly solid with many small anechoic spaces is seen. CT scan shows a hypodense mass with hyperdense septa of variable thickness. UESL is usually hypovascular with tumoral vessels. Some studies of UESL have demonstrated a large hepatic lesion with cystic appearance on CT/MRI with solid appearance on ultrasound highly suggestive of UESL.¹⁴

Pathological examination by Fine needle aspiration cytology followed by histopathological examination and immunohistochemistry is the mainstay in diagnosis of UES. Macroscopically UES is typically a large, single well circumscribed mass, greater than 10 cm in diameter, occasionally up to 35 cm. It is predominantly solid with foci of cystic or gelatinous degeneration, haemorrhage and necrosis.

Microscopically, loose or myxoid areas with variable cellularity, medium to large spindle, oval or stellate cells with poorly defined cell border, multinucleated giant cells with severe atypia are seen. Intracellular and extracellular diastase resistant PAS positive hyaline globules are seen. Some cases may show extramedullary hematopoiesis. Immunohistochemistry markers are variable for UES but help in exclusion of other tumors in the differential diagnosis.

Vimentin, CD 68 is positive, variable staining for glypican-3, CD 56, alpha-1 antitrypsin and alpha-chymotrypsin, cytokeratin give dot like staining. HepPar-1, S-100, GFAP, myoglobin, myogenin, MyoD1, Alk-1, CD 34, CD 117, smooth muscle myosin, heavy chain, h-caldesmon, PE 10, AFP are negative. CD 56 gives diffuse membranous expression, paranuclear dot like staining for cytokeratin in spindled pleomorphic and giant cells of UES help in differential diagnosis of abdominal masses in children and young adults.¹⁵

UES needs to be differentiated from embryonal rhabdomyosarcoma which shows positivity for Desmin, Myo D1, Myogenin, Extra skeletal ewing's sarcoma show positivity for CD 99, Unspecified sarcoma with focal positive for CK. UES is highly invasive malignant tumor with distant metastases. Lee et al, described a case of UESL in a child with distant metastases in the lung and adrenal glands.¹⁶ It shows amplification and deletion

of chromosomes 1q, 5p, 8p and 12q and a translocation of 19q13.¹⁷ Previously prognosis of UESL was poor but with the use of multimodal treatment including radiation therapy and chemotherapy prognosis has improved. Studies have shown improved survival rates ranging from 70-100 % in patients who were treated with multimodal therapy.¹⁸

CONCLUSION

To the best of our knowledge undifferentiated embryonal sarcoma has been described in the liver only. The present case of UES in a 9 year old Indian female is the FIRST in the EXTRAHEPATIC region. To emphasize the importance of cytology in the early diagnosis of UES with 100 % accuracy and confirmed by histopathology and IHC, aids in improving the survival rate when treated with multimodal therapy.

ACKNOWLEDGEMENTS

Authors would like to thank Patients.

Funding: No funding sources

Conflict of interest: None declared

Ethical approval: Not required

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Cite this article as: Rastogi N, Tanwar RK, Saxena B. Extrahepatic undifferentiated embryonal sarcoma, cytology as an accurate method for early diagnosis: an extremely rare case report in an Indian child. *Int J Res Med Sci* 2019;7:3175-9.